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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/364,908	07/27/1999	PHILIPPE MAINGAULT	43869/016200	1045

7590 03/19/2003

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EXAMINER	
WITZ, JEAN C	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/364,908	MAINGAULT ET AL
Examiner	**Art Unit**
Jean C. Witz	1651

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)[X] Responsive to communication(s) filed on *24 October 2002*.

2a)[X] This action is **FINAL**. 2b)[ ] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)[X] Claim(s) *17-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)[ ] Claim(s) _____ is/are allowed.

6)[X] Claim(s) *17-35* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)[ ] The specification is objected to by the Examiner.

10)[ ] The drawing(s) filed on _____ is/are: a)[ ] accepted or b)[ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)[ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[ ] All b)[ ] Some * c)[ ] None of:

1.[ ] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No. _____.

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) [ ] Interview Summary (PTO-413) Paper No(s) _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 24, 2003 has been entered.

Response to Arguments

Applicant's arguments filed October 24, 2002 have been fully considered but they are not persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 17-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Francesco et al. combined with WO 9637519.

The difference between the prior art and the claims as amended requires the production of the claimed product as a liquid, administering the liquid to a wound, the changing of the state of the product to a gel, and then the changing of the gel back into a liquid.

Applicants' arguments file October 24, 2002 do not address the fact that the prior art uses the same compositions as claimed for the same purpose, i.e. treatment of wounds. Therefore, the compositions would be expected to act in the same manner. The subsequent change in state of the product does not require any positive method steps and appears to be based upon the natural physiological conditions that exist in and around a wound. Applicants' arguments regarding the unsuitability of the opthalmological use of the referenced compositions are neither persuasive nor germane to the rejection of record. The disclosure of the prior art is in no way limited to opthalmological use and there is nothing in the claims that requires opthalmological use. Finally, obscuring vision does not negate any medicaments effectiveness in opthalmological uses; in fact, in most cases, it would be expected that the eye would be

bandaged after admiistration of a medicament so that obscured vision caused by the medicament is immaterial.

Applicants argue on March 18, 2002 that because Francesco does not explicitly teach reversibility, therefore, "Francesco teaches the use of irreversible gels." The claimed macromolecules (Applicants' wound-treatment product) are disclosed and fall well within the scope of the macromolecules produced by Francesco. Francesco teaches that a whole range of macromolecules may be produced and the sanitary surgical articles referenced by Applicants are only one embodiment of Francesco's invention. As stated in the previous office action, the reference of Francesco et al. teaches hydrogel compositions comprising esterified polysaccharide macromolecules (alginic acid or hyaluronic acid) with aliphatic chains which can exist either as a gel or can be solubilized. The aliphatic chains can be attached either via tetrabutyl ammonium salts of the carboxylic acid residues of the macromolecules or via esterification of the carboxylic acid residues with an aliphatic amine. The remaining carboxylic acid residues are converted to sodium salts. See, for example, Example 2 and Column 13, lines 15-50. The aliphatic chains are disclosed as preferably having 6 carbons. Therefore, Applicant's macromolecules are taught by the reference. It is not persuasive to assert that the teachings of a U.S. patent are limited only to one of its embodiments.

It is apparent that the esterified polysaccharide macromolecules are known to have gel properties as evidenced by the disclosure at col. 16, at lines 57-64, where the references states that "According to one particular aspect of the invention it is possible to prepare the medicaments of this type starting with the previously isolated and

possibly purified salts and, in their solid anhydrous state, as an amorphous powder, which on contact with the tissue to be treated constitute a concentrated aqueous solution of a gelatinous character with viscous consistency and elastic properties." (emphasis added). Therefore, the dry powder in contact with a wound surface will solubilize with the fluids found at the wound surface and form a gel.

Col. 36, lines 5-11 states that the macromolecules "in solid form come into contact with the epithelium to be treated, they form more or less concentrated solutions according to the nature of the particular epithelium to be treated, with the same characteristics as the solution previously prepared in vitro . . . ."

Therefore, the reversible physical nature of the molecules would have been readily apparent and known to one who would have practiced the invention as indicated supra, as clearly as the reversible physical nature of gelatin is readily apparent to anyone who prepares a solution of gelatin.

With regard to the WO 9637519 reference, Applicants again focus on a limited embodiment of the reference and fails to address the fact that the reference teaches hydrogel compositions comprising esterified polysaccharide macromolecules (alginic acid or hyaluronic acid) with aliphatic chains which can exist either as a gel or can be solubilized. The aliphatic chains are attached either via tetrabutyl ammonium salts of the carboxylic acid residues of the macromolecules. The remaining carboxylic acid residues are converted to sodium salts. It is inherent in the disclosure of this reference that these molecules that interactions occur between the aliphatic chains of various macromolecules. The aliphatic chains are disclosed as preferably having 6 carbons.

Once again, Applicants' macromolecules are taught. While the reference does not explicitly state that the product is to be applied as a solution and then caused to change into a gel state and then back into a liquid state, it is even clearer from the disclosure of this reference that one of ordinary skill in the art was aware not only of the changeability of the state of the alginate products and of the benefits of the gel state on a treated surface, but also aware of the use of the viscoelastic hydrogel as both a filler of tissue cavities and as a carrier for both medicaments and cells for the treatment of tissue cavities.

Again, as stated in the previous office action, the Examiner indicated that the reference does not explicitly state that the product is to be applied as a liquid, allowed to gel and then changed back into a liquid. However, the specification appears to be disclosing that the nature of the wound-site is sufficient to cause the change from liquid to gel then back to liquid. Applicants, at page 6, indicate that "pour[ing] the alginate system in the solution state onto the wound to be treated so that it conforms to the shape of the wound and comes into close contact with it. After a setting time the system gels and so adheres closely to the wound without the risk of running. Then under the effect of the ionic strength of the biological tissue medium and/or of the pH thereof, the alginate gel located in the proximity of the wound liquefies so that in spite of possible mechanical forces (changes in the wound, movement of the patient) the close contact between the treatment system and wound will always be maintained." Therefore, the gelation upon transfer to the wound site appears to occur without any further express, positive method step and the subsequent liquefaction is occurring in a limited manner in

a limited area, i.e. the wound-gel interface, such that the last "changing" step of the claims which calls for the liquefaction of the gel in situ in the wound, is also not an express, definitive action performed in the practice of the method; but, instead, this step is the natural progression and result of the application of the composition either in liquid or gel form, to a wound. In this case, Applicants' criticism of the use of the reversible gel as an ophthalmic treatment resulting in liquefaction such that vision is not possible is does not appear to be a true drawback of the application of the gel to the eye surface. Based upon Applicants' specification, the composition would not completely liquefy and it appears immaterial if vision is occluded. Many ocular treatments occlude vision. Lack of vision occlusion is not required by the claims.

It is clear that partial esterification of alginic acid or hyaluronic acid with aliphatic chains is conventional and results in compositions that can be found in both a liquid state and a gel state. Both references engage in the same processes of producing the compositions as disclosed by Applicants and use aliphatic chains having myriad of different lengths and chemical character. Chains of about 6 carbons are conventionally used. These modified polysaccharide molecules can exist as hydrogels or in solution, and are conventionally used as delivery vehicles for medicaments and for support for transplantation of cells. It is clear that selecting the specific aliphatic chain and the degree of esterification is well within the skill of the practitioner such that optimization of specific gel-sol parameters as desired would have been obvious to one of ordinary skill in the art at the time the invention was made. Finally, the disclosures of both references clearly suggest that the adhesion and viscoelastic qualities of the gels make them

excellent fillers for tissue cavities and defects including wounds. The reversible nature of the molecules from the gel state to the solution state would have been readily apparent to one who produced the molecules of the prior art. Applicants' method is more appropriately defined as the application of the liquid to the wound site. The next two method steps occur as a natural progression and do not appear to involve any further positive method steps. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to apply the composition as a solution sufficiently liquid to encourage complete filling of the cavity and would have been aware that the "liquid" would then covert to a hydrogel. The subsequent liquefication at the wound-gel interface would also occur naturally and require no further positive method steps. It is further noted that the terms "liquid" and "gel" are relative terms such that a "gel" may be sufficiently pourable to be "liquid" in nature and a "liquid" may have sufficient viscosity to have a "gel"-like consistency. The claims require no specific characteristics other than being "liquid" or "gel".

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (703) 308-3073. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-Th and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jean C. Witz
Primary Examiner
Art Unit 1651

March 18, 2003